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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/759,576 | 01/16/2004 | Jian-Bing Fan | 067234-0104 | 8734 |

41552 7590 03/24/2009

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| EXAMINER | |
|---|---|
| FORMAN, BETTY J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1634 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 03/24/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/759,576 | FAN ET AL. | |
| | Examiner | Art Unit | |
| | BJ Forman | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,4,6,8-10,14,16,25-28,31,33,37 and 39-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,6,8-10,14,16,25-28,31,33,37 and 39-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 14 January 2009 has been entered.

### *Status of the Claims*

2. This action is in response to papers filed 14 January 2009 in which claims 1, 14, 16, 25-28, 31, 33, 37 were amended, claims 18, 20-2, 38 were canceled and claims 39-50 were added. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action dated 18 July 2008 are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection are discussed.

Claims 1, 4, 6, 8-10, 14, 16, 25-28, 31, 33, 37, 39-50 are under prosecution.

### *Claim Rejections - 35 USC § 103*

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1, 4, 6, 8-10, 14, 16, 25-28, 31, 33, 37, 39, 41-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuber (U.S. Patent No. 5,571,676 issued 5 November 1996) and Walt et al (U.S. Patent No. 6,327,410, filed 11 Sept 1998) or Drmanac et al (EP 0392546, published 17 October 1990).

Regarding Claims 1 and 28, Shuber teaches an array comprising a substrate having microspheres distributed on the substrate (i.e. microtiter plate, Column 11, line 24), a population of microspheres wherein a first microsphere has a plurality of different target analytes from a first individual and second microsphere has a plurality of different target analytes from a second individual (i.e. amplification products from 5 primers sets, Example 1, Column 10, line 53-Column 11, line 11 and lines 23-25). Shuber does not teach the microspheres also have identifier binding ligands for identifying the individuals.

Walt et al teach a similar array composition comprising a substrate having discrete sites and a population of microspheres comprising a first and second microsphere, each microsphere comprising a plurality of target analytes covalently attached (i.e. bioactive agents, column 11, lines 41-45, 57-67) wherein the first and second microsphere have analytes from a different target source (e.g. rabbit, goat, mouse, Column 27, lines 30-60) wherein the microspheres are each encoded with an identifier to identify the analyte (Fig. 3 and Column 27, lines 30-60) and wherein the microspheres are distributed on the surface (Column 4, lines 35-50).

Walt et al further teaches preferred target analytes are genomic DNA (Column 10, lines 38-42) and teaches the preferred embodiment wherein each microsphere has a single type of analyte (Column 11, lines 41-43). The preferred embodiment taught by Walt inherently teaches embodiments other than the preferred embodiment because "preferred" is a comparative term used to describe the embodiment relative to an alternative less-preferred embodiment.

However, Shuber teaches the embodiment wherein the microspheres have multiple analytes different analytes whereby multiple genomic regions relative to cystic fibrosis are amplified and immobilized onto microsphere for simultaneous analysis of the disease-causing gene sequences (Examples 1-5 and Claims 17-18).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the microspheres of Shuber comprising multiple and different analytes to the microsphere array of Walt. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success and for the expected benefit of simultaneous analysis of disease-causing gene sequences as desired in the art (Shuber, Column 9, lines 18-39).

Alternatively, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the microspheres of Shuber by adding the identifiers of Walt (Column 4, lines 48-58) thereby providing an fast and inexpensive process for making and using the array. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success and for the benefit of fast

and inexpensive manufacture and use of the array as taught by Walt (Column 4, lines 53-55).

Furthermore, Drmanac teaches a similar composition comprising a first and second microsphere (discrete particle, (DP)), each comprising amplification product from fragmented genomic DNA, thus teaching different analytes on each DP (column 12 and column 13, lines 14-19) and labeled with an identifier binding ligands (Column 13, line 23-60).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the microspheres of Shuber and/or Walt et al by attaching the genomic fragments encoded by identifier oligos as taught by Drmanac. One of ordinary skill in the art would have been motivated to do so for the expected benefit of low cost and high throughput sequence determination as taught by Drmanac (Abstract and Column 1, lines 26-32). It would have been further obvious to one of ordinary skill to encode the microspheres of Shuber and/or Walt with the identifier binding ligands of Drmanac for the expected benefit of fast and frugal data generation (Column 4, lines 33-38).

Regarding Claims 4 and 31, Drmanac teaches the identifier binding ligands are nucleic acids (Column 7, line 51-Column 8, line 17).

Regarding Claims 6, 33, 42, 45, Shuber teach the array wherein the analytes are genomic DNA (Abstract, Example 1). Walt et al also teach the analytes are genomic DNA (Column 10, line 31). And Drmanac teaches the array wherein the analytes are genomic DNA (Abstract).

Regarding Claim 8, Walt et al disclose the array wherein the substrate is a fiber optic (Column 5, lines 24-31).

Regarding Claim 9, Shuber teaches the array wherein the substrate is plastic i.e. microtiter plate (Column 11, line 24). Walt et al disclose the array wherein the substrate is plastic (Column 5, lines 37-40).

Regarding Claim 10, Shuber teaches the array wherein the substrate has wells i.e. microtiter plate (Column 11, line 24). Walt et al disclose the array wherein the discrete sites are wells (Column 5, lines 61-67).

Regarding Claim 14, Walt et al teach the array wherein the surface comprises about 10,000 to 100,000,000 per $cm^2$ the discrete sites Column 5, lines 4-31).

Regarding Claims 16 and 47, Walt et al teach the array wherein the analytes are covalently attached to microspheres (Column 11, lines 63-64).

Regarding Claim 25, Walt et al disclose the composition wherein the surface comprises about 100,000 to 10,000,000 per $cm^2$ discrete sites (Column 5, lines 4-31).

Regarding Claim 26, Walt et al disclose the composition wherein the surface comprises about 10,000,000 to 1,000,000,000 per $cm^2$ discrete sites (Column 5, lines 5-31).

Regarding Claim 27, Walt et al disclose the composition wherein the surface comprises about 10,000 to 100,000 per $cm^2$ discrete sites (Column 5, lines 4-31).

Regarding Claims 37 and 48, Shuber teaches the array wherein the different analytes are amplification product using 5 different primer pairs, thereby producing at

least 2 different analytes (Column 10, lines 53-67) And Drmanac teaches a similar composition comprising a first and second microsphere (discrete particle, (DP)), each comprising amplification product from fragmented genomic DNA, thus teaching different analytes on each DP (column 12 and column 13, lines 14-19).

Regarding Claims 39 and 49, Shuber teaches the array wherein the different analytes are amplification product using 5 different primer pairs, thereby producing at least 10 different analytes (Column 10, lines 53-67).

Regarding Claims 41 and 44, Shuber teaches the array wherein the microspheres are distributed on the surface (Column 11, line 24). Walt et al teach the array wherein the microspheres are distributed on the surface (Column 4, lines 35-50). And Drmanac teaches the array wherein microspheres are distributed on the surface (column 7, lines 27-29).

Regarding Claims 43, 46, Shuber teach the array wherein the analytes are single stranded nucleic acids (i.e. denatured prior to hybridization, Column 11, lines 29-31). And Drmanac teaches the array wherein the nucleic acids are denatured prior to hybridization (Column 18, lines 45-58)

5. Claims 40 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuber (U.S. Patent No. 5,571,676 issued 5 November 1996) and Walt et al (U.S. Patent No. 6,327,410, filed 11 Sept 1998) or Drmanac et al (EP 0392546, published 17

October 1990) as applied to Claims 1 and 28 above and further in view of Shuber et al (Human Molecular Genetics, 1997, 6(3): 337-347).

Regarding Claims 40 and 50, Shuber teaches the array wherein the different analytes are amplification product using 5 different primer pairs, thereby producing at least 10 different analytes (Column 10, lines 53-67) and further teaches the method is applicable to multiple allele-specific targets (Column 3, lines 26-35) but does not specifically teach 100 targets. However, Shuber et al teach a similar composition wherein the allele-specific target analytes number more than 100 (Abstract). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the known allele-specific targets taught by Shuber et al to the array composition of Shuber, Walt and/or Drmanac. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success for the benefit of multiplex mutation analysis coupled with multiplex sample analysis as desired in the art (Shuber et al, page 343, right column, second full paragraph).

## ***Conclusion***

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BJ Forman
Primary Examiner
Art Unit 1634

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